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Pesticide Registration (PR) Notice 00-?

NOTICE TO MANUFACTURERS, FORMULATORS, PRODUCERS AND REGISTRANTS OF PESTICIDE PRODUCTS

ATTENTION: Persons Responsible for Registration of Pesticide Products

SUBJECT: [Draft] Guidance for Pesticide Registrants on Voluntary Pesticide Resistance Management Labeling Based on Mode/Target Site of Action on the Pest

The Office of Pesticide Programs (OPP) of the United States Environmental Protection Agency (EPA) announces voluntary pesticide resistance management labeling guidelines based on mode/target site of action for agricultural uses of herbicides, fungicides, bactericides, insecticides, and acaricides. This document provides recommended schemes of classification of pesticides according to their mode/target site of action (Appendices I-III), a standard format for showing group identification symbols on the end-use product labels, and guidelines for labeling resistance management strategies in the use directions. These guidelines are the result of a joint effort of the U.S., Canada, and Mexico under the North American Free Trade Agreement (NAFTA).

I. Scope

This Pesticide Registration (PR) notice is directed to registrants of herbicide, fungicide bactericide, insecticide, and acaricide products that are intended for general agricultural use, including both new products and old (existing) products and is not mandatory.

II. Introduction

The United States Environmental Protection Agency (EPA), Pest Management Regulatory Agency of Canada (PMRA) and Cicoplafest of Mexico are committed to long-term pest resistance management through pesticide resistance management and alternative pest management strategies. Under the auspices of the North American Free Trade Agreement (NAFTA), the U.S., Canada, and Mexico have joined together to develop and publish guidelines for voluntary pesticide resistance management labeling for implementation in North America. The development of these guidelines is part of the activities of the Risk Reduction Subcommittee of the NAFTA Technical Working Group on Pesticides. A uniform approach across North America will help reduce the development of pesticide resistance and support joint registration decisions by providing consistency in resistance management labeling being considered for approval in any or all of the NAFTA countries.

Pesticide resistance, defined for the purpose of this document as a heritable and significant decrease in the sensitivity of a pest population to a pesticide, reduces the field performance of pesticides. Pests covered by this initiative include insects, mites, weeds, and fungi and bacteria which cause plant disease. The management of pesticide resistance development is an important part of sustainable pest management and this, in conjunction with alternative pest management strategies and Integrated Pest Management (IPM) programs, can make significant contributions to reducing risks to humans and the environment. In support of this goal, the purpose of this document is to provide guidance on resistance management labeling to registrants.

Pesticides are important pest management tools. Many pesticides have gradually lost their effectiveness due to the development of resistance by pests. An important pesticide resistance management strategy is to avoid the repeated use of a particular pesticide, or pesticides that have a similar mode/target site of action as the pest control mechanism in the same field. Mode/target site of action refers to the biochemical mechanism by which the pesticide acts on the pest and should not be interpreted to imply that these chemicals share a common mechanism for purposes of cumulative human health risk assessment under the Food Quality Protection Act[1]. Rotating pesticides with a different mode/target site of action as the pest control mechanism will slow the development and subsequent buildup of this important type of resistance, mode/target site of action resistance, without resorting to increased rates and frequency of application and will prolong the useful life of many pesticides.

A resistance management strategy should also consider more detailed information regarding cross-resistance between pesticides with different modes of action resulting from the development of other types of resistance (e.g., enhanced metabolism, reduced penetration, or behavior changes). Pests may not be cross-resistant based merely on mode/site of action. However, this labeling initiative will provide pesticide users with easy access to important information regarding mode of action/target site resistance, the cornerstone of most resistance management programs.

To ensure consistency in pesticide grouping and labeling, and to contribute to the management of the pesticide resistance problem, the following guidelines have been developed for agricultural uses of herbicides, fungicides, bactericides, insecticides, and acaricides. The following classification schemes are based on mode/target site of action.

[1]Common mechanism of toxicity for purposes of cumulative human health risk assessment under FQPA is described in detail in EPA's guidance document "Guidance for identifying pesticide chemicals and other substances that have a common mechanism of toxicity" located at http://www.epa.gov/fedrgstr/EPA-PEST/1999/February/Day-05/6055.pdf.

III. Presentation and Format of Resistance Management Information on Pesticide Labels

The following format and presentation are recommended if registrants choose to include resistance management information on labels.

A. Mode of Action/Site of Action Grouping and Identification Symbol

Herbicides, fungicides, bactericides, insecticides, and acaricides are separately grouped according to their mode of action (or target site of action) by various technical/research committees consisting of representatives of the pesticide industry, researchers, extension specialists and regulatory officials. The industry committees providing guidance on the pesticide groupings were the: Herbicide Resistance Action Committee (HRAC), Fungicide Resistance Action Committee (FRAC), and Insecticide Resistance Action Committee (IRAC). Primary guidance for herbicides was provided by the Weed Science Society of America (WSSA). The site of action groups plus the identifier numbers for herbicides, fungicides/bactericides, and insecticides/acaricides are located in Appendix I, II and III, respectively.

The mode/site of action identification symbol should be shown on all end-use product labels (except products for homeowner/residential uses) in a standard format as outlined below, and should:

1. be located on the front panel (preferably at the upper right corner), surrounded by a black rectangle;

2. be in black and on a white background except the site of action number(s) which is to be white on a black background with a clear white gap between the site of action numbers; and

3. include the words “GROUP” and “HERBICIDE” (or “FUNGICIDE” or “INSECTICIDE”) in capital letters, and between these words the number(s) representing the site of action group(s) of each active ingredient(s). Where a product has two or more active ingredients, and these are represented by two or more sites of action, then two or more appropriate site of action identifier numbers should be used. For products containing an active ingredient that has multiple sites of action, the letter "M" should be used to represent the site of action group. Alternatively, if sites of action are known, specify each site of action by the appropriate number.

Example 1: Product containing one or more active ingredients of the same site of action.

GROUP	1	HERBICIDE

Example 2: Product containing two or more active ingredients represented by two or more sites of action.

GROUP	1	2	3	HERBICIDES

Example 3: Pre-mixture of a fungicide and an insecticide.

GROUP	1	FUNGICIDE
GROUP	2	INSECTICIDE

B. Resistance Management Statement

Resistance management statements are recommended to be included in the general use directions for all end-use products except products for homeowner/residential uses for the control of weeds, plant pathogens (diseases), insects and arthropods under the heading "Resistance Management Recommendations." The section "Resistance Management Recommendations" should be segregated under the "General" portion of the "Use Directions" and preferably boxed. Product specific labeling is recommended. The recommended standard resistance management labeling statements listed below focus on the mitigation of pest resistance and should be used where applicable. Efforts should be made to include all appropriate active ingredients and products. These recommendations should also be included in any product-specific literature.

1. Herbicides

Recommended standard resistance management labeling statement for herbicides.

(Name of product) is a Group (site of action group number) herbicide. Any weed population may contain or develop plants naturally resistant to (name of product) and other Group (site of action group number) herbicides. The resistant biotypes may dominate the weed population if these herbicides are

used repeatedly in the same field. Other resistance mechanisms that are not linked to site of action, but specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance management strategies should be followed.

To delay herbicide resistance:

- Where possible, rotate the use of (name of product) or other Group (site of action group number) herbicides with different herbicide Groups that control the same weeds in a field.

- Use tank-mixtures with herbicides from a different Group when such use is permitted.

- Herbicide use should be based on an IPM program that includes scouting, historical information related to herbicide use and crop rotation, and considers tillage (or other mechanical), cultural, biological, and other chemical control practices.

- Monitor treated weed populations for resistance development.

- Prevent movement of resistant weed seeds to other fields by cleaning harvesting and tillage equipment and planting clean seed.

- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance management and/or integrated weed management recommendations for specific crops and weed biotypes.

Optional, if available to company:
[• For further information or to report suspected resistance contact (company representatives) at toll free number: _____ or at Internet site: _____.]

Note: The above is a standard statement for products containing one or more active ingredients from the same group. For products containing two or more active ingredients from different groups, the statement should be modified to reflect the situation. For example:

(Name of product) is both a Group (site of action group

number) and a Group (site of action group number) herbicide. Any weed population may contain plants naturally resistant to Group (site of action group number) and/or Group (site of action group number) herbicides. The resistant biotypes may dominate the weed population if these herbicides are used repeatedly in the same fields.

2. Fungicides and Bactericides

Recommended standard resistance management labeling statement for fungicides and bactericides.

(Name of product) contains a Group (group number) (fungicide/bactericide). Any (fungal/bacterial) population may contain individuals naturally resistant to (name of product) and other Group (group number) (fungicides/bactericides). A gradual or total loss of pest control may occur over time if these (fungicides/bactericides) are used repeatedly in the same fields. Other resistance mechanisms that are not linked to site of action but specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance management strategies should be followed.

To delay fungicide/bactericide resistance:

- Where possible, rotate the use of (name of product) or other Group (site of action group number) fungicides/bactericides with different Groups that control the same pathogens.

  This statement may be modified if repeated and/or successive application is necessary, e.g., Avoid application of more than (maximum number) and consecutive sprays (maximum number) of (name of product) or other (fungicides/bactericides) in the same group in a season.

- Use tank-mixtures with fungicide/bactericides from a different Group when such use is permitted.

- Fungicide/bactericide use should be based on an IPM program that includes scouting, historical information related to pesticide use and crop rotation, and considers cultural, biological, and other chemical control practices.

- Monitor treated fungal/bacterial populations for resistance

development.

• If disease continues to progress after treatment with this product, do not increase the use rate beyond label rate. Discontinue use of this product and switch to another (fungicide/bactericide) with a different target site of action, if available.

• Contact your local extension specialist or certified crop advisors for any additional pesticide resistance management and/or IPM recommendations for specific crops and pathogens.

Optional, if available to company:
[• For further information or to report suspected resistance contact (company representatives) at toll free number: _____ or at Internet site: _____.]

Note: The above is a standard statement for products containing one or more active ingredients from the same group. For products containing two or more active ingredients from different groups, the statement should be modified to reflect the situation. For example:

> (Name of product) contains both a Group (group number) and Group (group number) fungicide/bactericide. Any fungal/bacterial population may contain individuals naturally resistant to (name of product) and other Group (group number) or Group (group number) fungicides/bactericides. A gradual or total loss of pest control may occur over time if these (fungicides/bactericides) are used repeatedly in the same fields.

3. Insecticides and Acaricides

Recommended standard resistance management labeling statement for insecticides and acaricides.

(Name of product) contains a Group (group number) insecticide (or acaricide). Any (insect/mite) population may contain individuals naturally resistant to (name of product) and other Group (group number) (insecticides/acaricides). The resistant individuals may dominate the insect/mite population if this group of insecticides/acaricides are used repeatedly in the same fields. Other resistance mechanisms that are not

linked to site of action but are specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance management strategies should be followed.

To delay insecticide (or acaricide) resistance:

- Where possible, rotate the use of (name of product) or other Group (site of action group number) insecticides/acaricides with different Groups that control the same pests in a field.

  The above statement may be modified on a pest by pest basis if a number of applications each year are necessary, e.g., Avoid application of more than (maximum number) and consecutive sprays of (name of product) or other insecticides in the same group in a season.

- Use tank-mixtures with insecticide/acaricides from a different Group when such use is permitted.

- Insecticide/acaricide use should be based on an IPM program that includes scouting, record-keeping, and considers cultural, biological, and other chemical control practices.

- Monitor treated insect/mite populations for resistance development.

- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance management and/or IPM recommendations for the specific site and pest problems in your area.

Optional, if available to company:
[• For further information or to report suspected resistance contact (company representatives) at toll free number: _____ or at Internet site: _____.]

Note: The above is a standard statement for products containing one or more active ingredients from the same group. For products containing two or more active ingredients from different groups, the statement should be modified to reflect the situation. For example:

(Name of product) contains both a Group (group number)

and Group (group number) insecticides/acaricides. Any insect/mite population may contain individuals naturally resistant to (name of product) and other Group (group number) or Group (group number) insecticides/acaricides. The resistant individuals may dominate the insect/mite population if these insecticides/acaricides are used repeatedly in the same fields.

4. Pesticides of Unspecified Groups or Pesticides Without History of Resistance

Some herbicides, fungicides, bactericides, insecticides, and acaricides have not been assigned to any particular mode/target site of action group, or have not been shown on the lists in this document because of the lack of clear understanding of their mode/target site of action or the absence of a history of resistance development for the product, e.g., nematicides. The registrants should establish the appropriate group identifications for their products in consultation with representatives of the pesticide industry, researchers, extension specialists and regulatory officials. The general use directions should include the appropriate resistance management statements for the product, i.e., herbicides, fungicides, bactericides, insecticides, and acaricides.

IV. Addition or Changes to Mode/ Site of Action Lists

The guidance in this notice applies to new products and existing products when they are registered for use. The pesticide lists will be updated from time to time (approximately annually) to include product names and/or new/revised target site/mode of action classification which will be added to the lists in the future (i.e., Appendices I-III) and be posted on the Office of Pesticide Program's home page under the title of this PR Notice or other identifiable heading. Hard copies will be made available from the Agency upon request.

V. Implementation

The implementation of this program is to be on a voluntary basis by the pesticide industry. Close cooperation of all registrants is required to achieve this important task. Registrants are encouraged to add the resistance management grouping symbols and statements to both new and existing product labels. All new and existing products are encouraged to have the resistance management grouping symbols and statements on the label by January 1, 2004. Specific guidance on amending your label can be obtained from the product manager. In view of the importance of resistance management to a long-term pest management strategy, the EPA will closely monitor the progress in the industry's

implementation of resistance management labeling.

VI. For Further Information

If you have questions about this PR Notice, please contact:

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Attachments:
Appendix I: Herbicide Groups Based on Mode/Target Site of Action
Appendix II: Fungicide/Bactericide Groups Based on Activity Group/Site of Action
Appendix III: Insecticide and Acaricide Groups Based on Mode/Target Site of Action

Appendix I: Herbicide Groups Based on Mode/Site of Action[1]

GROUP	MODE/ SITE OF ACTION	CHEMICAL FAMILY	ACTIVE INGREDIENT
1	Inhibitors of acetyl CoA carboxylase ACCase	Aryloxyphenoxy propionates	clodinafop-propargyl
			diclofop-methyl

GROUP	MODE/ SITE OF ACTION	CHEMICAL FAMILY	ACTIVE INGREDIENT
			fenoxaprop-ethyl
			fenoxaprop-p-ethyl
			fluazifop-p-butyl
			fluazifop-butyl
			quizalofop-ethyl
			quizalofop-p-ethyl
		Cyclohexanediones	clethodim
			sethoxydim
			tralkoxydim
2	Inhibition of acetolactate synthase ALS and also called aceto-hydroxyacid synthase AHAS	Sulfonylureas	bensulfuron
			chlorimuron
			chlorsulfuron
			ethametsulfuron-methyl
			halosulfuron-methyl
			metsulfuron-methyl
			nicosulfuron
			primisulfuron
			prosulfuron
			rimsulfuron
			sulfometuron
			sulfosulfuron
			thifensulfuron-methyl
			triasulfuron
			tribenuron-methyl
			triflusulfuron-methyl
		Imidazolinones	imazamethabenz

GROUP	MODE/ SITE OF ACTION	CHEMICAL FAMILY	ACTIVE INGREDIENT
			imazamox
			imazapyr
			imazethapyr
		Pyrimidinylthio-benzoate	pyrithiobac sodium
		Triazolo-pyrimidime	flumetsulam
3	Microtubule assembly inhibitors	Dinitroanilines	benfluralin
			ethalfluralin
			pendimethalin
			trifluralin
		Pyridazine	dithiopyr
			thiazopyr
	Unknown	None	chlorthal-dimethyl (DCPA)
4	Synthetic auxins (action like indoleacetic acid)	Phenoxys	2,4-D
			2,4-DB
			dichlorprop (2,4-DP)
			MCPA
			MCPB
			mecoprop (MCPP)
		Benzoic acids	dicamba
		Pyridine carboxylic acids	clopyralid
			fluroxypyr
			picloram
			triclopyr
		Quinoline carboxylic acid	quinclorac

GROUP	MODE/ SITE OF ACTION	CHEMICAL FAMILY	ACTIVE INGREDIENT
		Semicarbazone	diflufenzopyr
5	Inhibitors of photo-synthesis at photosystem II Site A	Triazines	ametryn
			atrazine
			cyanazine
			prometon
			prometryn
			propazine
			simazine
		Triazinones	hexazinone
			metribuzin
		Uracils	bromacil
			terbacil
		Pyridazinone	pyrazon
		Phenyl-carbamates	desmedipham
			phenmedipham
6	Similar to group 5, but different binding behavior	Nitriles	bromoxynil
			ioxynil
		Benzothia-diazoles	bentazon
		Phenyl-pyridazine	pyridate
7	Inhibitors of photo-synthesis at photosystem II Site B	Ureas	diuron
			fluometuron
			linuron
			metobromuron
			monolinuron
			siduron

GROUP	MODE/ SITE OF ACTION	CHEMICAL FAMILY	ACTIVE INGREDIENT
			tebuthiuron
		Amide	propanil
8	Inhibition of lipid synthesis - not ACCase inhibition	Thiocarbamates	butylate
			cycloate
			EPTC
			pebulate
			thiobencarb
			triallate
			vernolate
		None generally accepted	bensulide
	Unknown	None generally accepted	difenzoquat
9	Inhibitors of EPSP synthase	None generally accepted	glyphosate
10	Inhibitors of glutamine synthetase	None generally accepted	glufosinate-ammonium
11	Bleaching: Inhibitors of carotenoid biosynthesis (unknown target)	Triazole	amitrole
12	Bleaching: Inhibitors of carotenoid biosynthesis at the phytoene desaturase step (PDS)	Pyridazinone	norflurazon
		Nicotinanilide	diflufenican
		Others	fluridone
			flurochloridone
			flurtamone
13	Bleaching: Inhibition of all diterpenes	Isoxazolidinone	clomazone
14	Inhibitors of proto-porphyrinogen oxidase (PPO)	Diphenylethers	acifluorfen
			fomesafen

GROUP	MODE/ SITE OF ACTION	CHEMICAL FAMILY	ACTIVE INGREDIENT
			lactofen
			oxyfluorfen
		N-phenyl-phthalimides	fluthiacet-methyl
			flumiclorac-pentyl
		Oxadiazole	oxadiazon
		Triazolinone	carfentrazone-ethyl
			sulfentrazone
15	Unknown	Chloro-acetamides	acetochlor
			alachlor
			butachlor
			metolachlor
			s-metolachlor
			pronamide (propyzamid)
			propachlor
			demethenamid
		Acetamides	diphenamid
			napropamide
		Oxyacetamides	menenacet
			fluthiamide
16	Unknown	Benzofuran	ethofumesate
17	Unknown	Organo-arsenicals	Arsenic, present as disodium salt of methanearsonic acid (DSMA)
			Arsenic, present as monosodium salt of methanearsonic acid (MSMA)

GROUP	MODE/ SITE OF ACTION	CHEMICAL FAMILY	ACTIVE INGREDIENT
18	Inhibits DHP (dihydropteroate) synthase step	Carbamate	asulam
19	Inhibits indoleacetic acid action	Phthalamate	naptalam
20	Inhibits cell wall synthesis Site A	Nitrile	dichlobenil
21	Inhibits cell wall synthesis Site B	Benzamide	isoxaben
22	Photo system I- electron diverters	Bipyridyliums	diquat
			paraquat
23	Inhibitors of mitosis	Carbamates	chlorpropham
			propham
24	Uncoupling (ATP) membrane disruptors	Dinitrophenol	dinoseb[2]
25	Unknown	Arylamino- propionic acid	flamprop-methyl
26	Unknown	None generally accepted	trichloroacetic acid (TCA)
27	Unknown	Various	bromobutide
			cinmethylin
			dymron
			flupoxam
28	Inhibition of 4-hydroxy-phenyl-pyruvate-dioxygenase (4-HPPD)	Isoxazole	isoxaflutole
		Pyrazole	pyrazolynate
		Triketone	sulcotrione

[1] This list is based on the Herbicide Classification of the Weed Science Society of America (*Weed Technology*, 1997, 11:384-393). Microbial herbicides are not included.

[2] There are no active registered uses for dinoseb in the U.S.

Appendix II: Fungicide/Bactericide Groups Based on Activity Group/Site of Action[1]

GROUP	ACTIVITY GROUP/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
1	Inhibition of tubulin formation	Benzimadazoles	benomyl
			carbendazim
			thiabendazole
			thiophanate
			thiophanate-methyl
			fuberidazole
2	Affect cell division, DNA & RNA synthesis, & metabolism	Dicarboximides	iprodione
			procymidone
			vinclozolin
3	DMI (Demethylation Inhibitor): Inhibition of sterol synthesis	Imidazoles	imazalil
			perfurazoate
			prochloraz
			triflumizole
		Piperazine	triforine[2]
		Pyridine	pyrifenox
		Pyrimidines	fenarimol
			nuarimol
		Triazoles (includes conazoles)	bitertanol
			bromuconazole
			cyproconazole
			diclobutrazol
			difenoconazole

GROUP	ACTIVITY GROUP/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
			diniconazole
			epoxiconazole
			fenbuconazole
			fluquinconazole
			flusilazole
			flutriafol
			hexaconazole
			metconazole
			myclobutanil
			paclobutrazol
			penconazole
			propiconazole
			tebuconazole
			tetraconazole
			triadimefon
			triadimenol
			triticonazole
4	Phenylamides-Affect RNA synthesis	Acylamines	benalaxyl
			furalaxyl
			metalaxyl
			m-metalaxyl
		Oxazolidinones	oxadixyl
		Butyrolactones	ofurace
5	Morpholines	Morpholines	aldimorph
			fenpropimorph
			tridemorph

GROUP	ACTIVITY GROUP/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
		Piperidine	fenpropidin
		Spiroketalamine	spiroxamine
6	Phosphoro-thiolate	Organophosphorous	edifenphos
			iprobenfos (IBP)
			isoprothiolane
			pyrazophos
7	Oxathiin: Affect mitochondrial transport chain	Anilide (Oxathiin)	bendodanil
			carboxin
			flutolanil
			mepronil
			oxycarboxin
8	Hydroxy-primidine	Pyrimidinol	bupirimate
			dimethirimol
			ethirimol
9	Anilino-pyrimidine	Anilinopyrimidine	cyprodinil
			mepanipyrim
			pyrimethanil
10	N-Phenyl-carbamates	Diethofencarb	diethofencarb
11	Strobilurin Type Action and Resistance (STAR)	Strobilurins: Methoxyacrylate	azoxystrobin
		Oximinioacetate	kresoxim-methyl
			trifloxystrobin
		Non-strobilurins: Oxazolidinedione	famoxadone

Appendix II

GROUP	ACTIVITY GROUP/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
12	Phenylpyrroles	Phenylpyrroles	fenpiclonil
			fludioxonil
13	Quinolines	Quinoline	quinoxyfen
14	Aromatic hydrocarbons	Chlorophenyls	biphenyl
			chloroneb
			dicloran (DCNA)
			etridiazole
			quintozene
			tecnazene
			tolclofos-methyl
15	Cinnamic acids	Cinnamic acid	dimethomorph
16	Melanin Biosynthesis Inhibitors (MBI)	Reductase inhibitors	fthalide
			pryoquilon
			tricyclazole
		Dehydratase inhibitor	carpropamid
17	Hydroxyanilide	Hydroxyanilide	fenhexamid
18	Antibiotics		blasticidin
			kasugamycin
			oxytetracycline[3]
			streptomycin
			validamycin
19	Polyoxins		polyoxin
20	Phenylurea		pencycuron
21	Plant host defense inducers Be	Benzothiadiazole (BTH)	acibenzolar-S-methyl
			carpropamid
			probenazole

GROUP	ACTIVITY GROUP/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
U[4]	Unknown Miscellaneous	Amino acid amide	iprovalicarb
		Carbamate	iodocarb
			propamocarb
		Cyano-acetamide oxime	cymoxanil
		Organo-tins	tri-phenyl tins
			dinocap
			fenfuram
			fosetyl-aluminum
M[5]	Multi-site activity	Inorganics	aresenates
			copper (plus salts)
			sulphur
		Dithiocarbamates and relatives	ferbam
			mancozeb
			maneb
			metiram
			propineb
			thiram
			zineb
			ziram
		Chloroalkythios	captan
			folpet
		Chloronitrile	chlorothalonil
		Sulphamides	dichlofluanid
			tolyfluanid

GROUP	ACTIVITY GROUP/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
		Guanidines	dodine
			guazatine
			iminoctadine
		Anilazine	anilazine
		Quinone	dithianon
		Phenyl-pyridinamine	fluazinam

[1] This list is based on the fungicide listing compiled by the Fungicide Resistance Action Committee (FRAC). FRAC is a Specialist Technical Group of the Global Crop Protection Federation (GCPF). Microbial fungicides, e.g. *Bacillus subtilis*, or *Agrobacterium radiobacter* K84, are not included.

[2] There are no active registered uses for triforine in the U.S.

[3] Only Section 18 use on apples.

[4] The Unknown group, designated by symbol “U,” comprises a set of miscellaneous compounds for which that biochemical mode of action may or may not be known, but are not able to placed with certainty in any other groupings.

[5] The Multi-site activity grouping, designatd by symbol "M," comprises a collection of various chemicals that act as general toxophores with several sites of action. These sites may differ between group members.

Appendix III: Insecticide and Acaricide Groups Based on Mode/Site of Action[1]

GROUP	MODE/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
1A[2]	*Acetyl choline esterase inhibitors* Inhibition of the enzyme acetylcholinesterase, interrupting the transmission of nerve impulses.	Carbamates	aldicarb
			aminocarb
			bendiocarb
			carbaryl
			carbofuran
			formetanate hydrochloride
			methiocarb
			methomyl
			oxamyl
			pirimicarb
			propoxur
1B[2]		Organo-phosphates	acephate
			azamethiphos
			azinphos-methyl
			chlorfenvinphos
			chlorpyrifos
			coumaphos
			diazinon
			dichlorvos/DDVP
			dicrotophos
			dimethoate
			disulfoton
			ethion
			fenitrothion
			fensulfothion
			fenthion
			fonofos
			malathion
			methamidophos

GROUP	MODE/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
			methidathion
			naled
			oxydemeton-methyl
			parathion
			phorate
			phosalone
			phosmet
			pyrazophos
			sulfotep
			tebupirimfos
			temephos
			terbufos
			tetrachlorvinphos
			trichlorfon
2A[2]	*GABA-gated chloride channel antagonists* Interferes with GABA receptors of insect neurons, leading to repetitive nervous discharges	Chlorinated Cyclodienes and Polychlorocycloalkanes	dicofol
			endosulfan
			lindane
			methoxychlor
2B[2]	*GABA-gated chloride channel antagonists* Interferes with GABA receptors of insect neurons, leading to repetitive nervous discharges- fiprole site	Phenylpyrazoles	fipronil
3	*Sodium channel modulators* Acts as an axonic poison by interfering with the sodium channels of both the peripheral and central nervous system stimulating repetitive nervous discharges, leading to paralysis.	Synthetic Pyrethroids	allethrin
			d-cis-trans allethrin
			d-trans allethrin
			cyfluthrin
			beta-cyfluthrin
			lambda-cyhalothrin
			cypermethrin
			alpha-cypermethrin

GROUP	MODE/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
			beta-cypermethrin
			theta-cypermethrin
			zeta-cypermethrin
			deltamethrin
			fenpropathrin
			fenvalerate
			flucythrinate
			tau-fluvalinate
			permethrin
			resmethrin
			tefluthrin
			tetramethrin
			d-tetramethrin
		Pyrethrins	pyrethrins
4	*Acetylcholine receptor agonists/antagonists* Binds to nicotinic acetylcholine receptor, disrupting nerve transmission	Chloronicotines (nitro-guanidines)	imidacloprid
		Nicotine, Cartap, Bensultap	nicotine
			cartap
			bensultap
5	*Acetylcholine receptor modulators* Alters acetylcholine receptor site and disrupts binding	Spinosyns	spinosyns
6	*Chloride channel activators* Interferes with the GABA nerve receptor of insects.	Avermectin	abamectin
			enamectin benzoate
		Milbemycin	mibemycin
7	*Juvenile hormone mimics (Insect growth regulator)* Mimic juvenile hormones which prevent moulting from the larval to the adult stage.	Juvenile hormone analogues	fenoxycarb
			hydroprene
			methoprene
			pyriproxifen
8A[2]	*Unknown or Non- specific site of action (fumigants)*	Fumigant	methyl bromide

8B[2]			aluminum phosphide
8C[2]			ethylene dibromide
9A[2]	*Compounds of unknown or non-specific site of action (feeding disrupters)*	Feeding Disruptors	pymetrozine
9B[2]			cryolite
10	*Compounds of unknown or non-specific site of action (mite growth inhibitors)*	Mite Growth Inhibitors (Ovicide)	clofentezine
			hexythiazox
11A	*Microbial disruptors of insect midgut membranes (includes Cry proteins expressed in transgenic plants)* Organism has protein inclusions that are released in the gut of the target pest resulting in gut paralysis and a cessation of feeding.	Bt Microbials (Biological insecticide/larvicide) - Dipteran specific	*Bacillus thuringiensis* var. *israelensis*
			Bacillus sphaericus
11B		Bt Microbials (Biological insecticide/larvicide) - Lepidopteran specific	*Bacillus thuringiensis var. aizawai*
			Bacillus thuringiensis var. aizawai, encapsulated delta endotoxin
			Bacillus thuringiensis var. *kurstaki*
			Bacillus thuringiensis var. kurstaki encapsulated delta endotoxin
11C		Bt Microbials (Biological insecticide/larvicide) - Coleopteran specific	*Bacillus thuringiensis* var. *tenebrionis*
			Bacillus thuringiensis var. *tenebrionis* encapsulated delta endotoxin
12	*Inhibition of oxidative phosphorylation at the site of dinitrophenol uncoupling (disrupt ATP formation)*	Organotin Miticide	fenbutatin oxide
GROUP	**MODE/SITE OF ACTION**	**CHEMICAL GROUP**	**ACTIVE INGREDIENT**
13	*Uncoupler of oxidative phosphorylation (disrupt H proton gradient formation)*	Pyrrole compound (Broad spectrum contact and stomach poison)	chorfenapyr*
14	*Inhibit magnesium- stimulated ATPase*	Sulfite Ester Miticide	propargite

GROUP	MODE/SITE OF ACTION	CHEMICAL GROUP	ACTIVE INGREDIENT
13	*Uncoupler of oxidative phosphorylation (disrupt H proton gradient formation)*	Pyrrole compound (Broad spectrum contact and stomach poison)	chorfenapyr*
15	*Inhibit chitin biosynthesis*	Substituted benzoylurea	diflubenzuron
16	*Inhibit chitin biosynthesis type 1 - Homopteran*	Thiadiazine	buprofezin
17	*Inhibit chitin biosynthesis type 2- Dipteran*	Triazine	cyromazine
18	*Ecdysone agonist/disruptor* Disrupts insect molting by antagonizing the insect hormone ecdysone	Benzoic acid hydrazide	tebufenozide
		Botanical (Neem oil or azadirachtin)	Neem oil or azadirachtin
19	*Octopaminergic agonist*	Triazapentadiene	amitraz
20	*Site II electron transport inhibitors*	None	diafenthiuron
			hydramethylnon
21	*Site I electron transport inhibitors*	Botanical	rotenone
		Pyridazinone	pyridaben

[1] The classification scheme was developed in consultation with the Insecticide Resistance Action Committee (IRAC). IRAC is a Specialist Technical Group of the Global Crop Protection Federation (GCPF). It is recognized that resistance of insects and mites to insecticides and acaricides can also result from enhanced metabolism, reduced penetration or behavioral changes that are not linked to any site of action classification, but are specific for individual chemicals or chemical groups. All members of a class may not be cross-resistant based merely on mode of action. Most biological insecticides are not included in this Appendix because they are thought not to pose as great a concern for resistance development. Microbial products involving Cry delta-endotoxins from *Bacillus* sp. are included as well as biochemical products derived from the Neem tree such as azadirachtin.

[2] Other resistance mechanisms that are not linked to site of action, such as enhanced metabolism, are common for this group of chemicals. All members of this class may not have developed significant cross-resistance. When only this group of products are available, alternation of compounds from subgroup A and subgroup B are recommended.

[3] Use under Section 18 only.